Remarks

By the present communication, the specification and claim 11 have been amended to include sequence identifiers in compliance with sequence disclosure requirements under 37 C.F.R. § 1.821 - 1.825. Attached hereto is a marked-up version of the changes made to the specification and the claims, labeled APPENDIX A. A clean copy of the complete set of all pending claims for this application, claims 1-19, is also provided for the Examiner's convenience in APPENDIX B.

In view of the above amendments and remarks, prompt and favorable action on all pending claims is respectfully requested. In the event any matters remain to be resolved in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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Enclosures: Appendices A and B

APPENDIX A – ALTERED SPECIFICATION AND CLAIMS
VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

Paragraph **[0028]** on page 9 has been amended as follows:

[0028] The FLP recombination target site (sometimes referred to herein as "FRT") has also been identified as minimally comprising two 13 base-pair repeats, separated by an 8 base-pair spacer, as follows:

-Spacer-
5' - GAAGTTCCTATTC[TCTAGAAA]GTATAGGAACTTC - 3' **(SEQ ID NO:3)**
Xba I site

The nucleotides in the above "spacer" region can be replaced with any other combination of nucleotides, so long as the two 13 base-pair repeats are separated by 8 nucleotides. The actual nucleotide sequence of the spacer is not critical, although those of skill in the art recognize that, for some applications, it is desirable for the spacer to be asymmetric, while for other applications, a symmetrical spacer can be employed. Generally, the spacers of the FLP recombination target sites undergoing recombination with one another will be the same.

Paragraph **[0047]** on page 14 has been amended as follows:

[0047] pFRTβGAL contains a version of the bacterial β-galactosidase sequence modified by insertion of a FLP recombination target site, or FRT, within the protein coding sequence immediately 3' to the translational start. The oligonucleotide used for the construction of pFRTβGAL was:

5' - GATCCCGGGCTACC**ATG**GA GAAGTTCCTATTC CGAAGTTCCTATTC
(TCTAGA)AAGTATAGGAACTTCA - 3' **(SEQ ID NO:4)**.

This oligonucleotide contains an in-frame start codon, minimal FRT site, and an additional copy of the 13-bp FRT repeat [°XXX°]; the XbaI site within the FRT spacer is enclosed in parentheses. The linker was inserted between the BamHI and HindIII sites of pSKS105 (Casadaban et al., *Meth. Enzymol.* **100**:293, 1983) and the LacZ portion of modified gene was cloned into a pSV2 vector. The neomycin cassette used for construction of pNEOβGAL was an XhoI to BamHI fragment from pMC1neo-polyA (Thomas and Capecchi, *Cell* **51**:503, 1987) cloned between copies of the J3 FRT site in pUC19.

In the claims:

Claim 11 has been amended as follows:

11. (Amended) A transgenic, non-human mammal according to claim 1, wherein said FLP recombination target site has the sequence:

5' - GAAGTTCCTATTCTCTAGAAAGTATAGGAACTTC - 3' (SEQ ID NO:3),

or functional equivalents thereof.

APPENDIX B – COMPLETE SET OF PENDING CLAIMS

1. A transgenic, non-human mammal, wherein said mammal contains at least one FLP recombination target site in the genomic DNA thereof.

2. A transgenic, non-human mammal according to claim 1, wherein said FLP recombination target site is positioned within at least a portion of one or more gene(s) of interest.

3. A transgenic, non-human mammal according to claim 1, further comprising a nucleotide sequence encoding, and capable of expressing, in transgenic, non-human mammals, a FLP recombinase.

4. A transgenic, non-human mammal according to claim 1, further comprising FLP recombinase.

5. A transgenic, non-human mammal according to claim 1, wherein said mammal is a mouse.

6. A transgenic, non-human mammal according to claim 1, wherein said mammal is a rat.

7. A transgenic, non-human mammal according to claim 1, wherein said mammal is a monkey.

8. A transgenic, non-human mammal according to claim 1, wherein said mammal is a hamster.

9. A transgenic, non-human mammal according to claim 2, wherein said gene(s) of interest provide a readily analyzable marker feature to the host system.

10. A transgenic, non-human mammal according to claim 9, wherein said marker is selected from the group consisting of β-galactosidase, thymidine kinase, tyrosinase, and antibiotic resistance.

11. (Amended) A transgenic, non-human mammal according to claim 1, wherein said FLP recombination target site has the sequence:

5' - GAAGTTCCTATTCTCTAGAAAGTATAGGAACTTC - 3' (SEQ ID NO:3),

or functional equivalents thereof.

12. A transgenic, non-human mammal according to claim 2, further comprising an additional DNA fragment, wherein said additional DNA fragment is selected from:

(a) at least a second portion of said first gene of interest, or

(b) at least a portion of a second gene of interest;

wherein said second DNA contains at least one FLP recombination target site; and wherein said second DNA, when combined in reading frame with said first DNA, provides a functional gene.

13. A transgenic, non-human mammal according to claim 2, further comprising an additional DNA fragment, wherein said additional DNA fragment is selected from:

(a) at least a second portion of said first gene of interest, or

(b) at least a portion of a second gene of interest;

wherein said second DNA contains at least one FLP recombination target site; and wherein site-specific recombination disrupts the function of said first gene of interest.

14. A transgenic, non-human mammal according to claim 13, wherein said function is colorimetrically detectable, immunologically detectable or genetically detectable.

15. A transgenic, non-human mammal according to claim 3, wherein said mammal is selected from the group consisting of a mouse, a rat, a monkey and a hamster.

16. A transgenic, non-human mammal according to claim 4, wherein said mammal is selected from the group consisting of a mouse, a rat, a monkey and a hamster.

17. A transgenic, non-human mammal according to claim 9, wherein said mammal is selected from the group consisting of a mouse, a rat, a monkey and a hamster.

18. A transgenic, non-human mammal according to claim 12, wherein said mammal is selected from the group consisting of a mouse, a rat, a monkey and a hamster.

19. A transgenic, non-human mammal according to claim 13, wherein said mammal is selected from the group consisting of a mouse, a rat, a monkey and a hamster.